Cost-Effectiveness of Lower Extremity Nerve Decompression Surgery in the Prevention of Ulcers and Amputations: A Markov Analysis

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Patient-reported Health

Background: The costs and health effects associated with lower extremity complications in diabetes mellitus are an increasing burden to society. In selected patients, lower extremity nerve decompression is able to reduce symptoms of neuropathy and the concomitant risks of diabetic foot ulcers and amputations. To estimate the health and economic effects of this type of surgery, the cost-effectiveness of this intervention compared to current nonsurgical care was studied.

Methods: To estimate the incremental cost-effectiveness of lower extremity nerve decompression over a 10-year period, a Markov model was developed to simulate the onset and progression of diabetic foot disease in patients with diabetes and neuropathy who underwent lower extremity nerve decompression surgery, compared to a group undergoing current nonsurgical care. Mean survival time, health-related quality of life, presence or risk of lower extremity complications, and in-hospital costs were the outcome measures assessed. Data from the Rotterdam Diabetic Foot Study were used as current care, complemented with information from international studies on the epidemiology of diabetic foot disease, resource use, and costs, to feed the model.

Results: Lower extremity nerve decompression surgery resulted in improved life expectancy (88,369.5 life-years versus 86,513.6 life-years), gain of quality-adjusted life-years (67,652.5 versus 64,082.3), and reduced incidence of foot complications compared to current care (490 versus 1087). The incremental cost-effectiveness analysis was −€59,279.6 per quality-adjusted life-year gained, which is below the Dutch critical threshold of less than €80,000 per quality-adjusted life-year.

Conclusions: Decompression surgery of lower extremity nerves improves survival, reduces diabetic foot complications, and is cost saving and cost-effective compared with current care, suggesting considerable socioeconomic benefit for society. (*Plast. Reconstr. Surg.* 148: 1135, 2021.)

The prevalence of diabetes mellitus has quadrupled since 1980, accounting for 422 million of cases in 2014, with the majority of the rise explained by increasing rates of diabetes in developing countries.[1] This number is expected to increase further in the years to come, which is directly related to the rising prevalence of obesity, sedentary lifestyle, and unhealthy diet, on top of the continuously expanding and aging global population.[2] Therefore, the number of complications of diabetes is also expected to increase. The burden of lower extremity complications as seen in diabetes mellitus is worrisome and expensive at both patient and society levels. The costs of diabetic neuropathy, foot ulceration, and lower extremity amputation are already immense, with reports of burden on public and private payers ranging from $9 to $13 billion in addition to the costs of diabetes itself.[3,4]

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Received for publication June 4, 2020; accepted February 9, 2021.

DOI: 10.1097/PRS.0000000000008440

Disclosure: *The authors have no financial interest to declare in relation to the content of this article. No funding was received for this work.*

To diminish the burden to society, various strategies have been implemented to reduce the incidence of new diabetic foot ulceration or deterioration into lower extremity amputation.[5,6] Regrettably, symptoms of neuropathy have proven to be tenacious, with few convincing long-term solutions available tackling the symptoms of neuropathy and its consequent fearsome sensory loss.[7] However, emerging evidence reveals that entrapped lower extremity nerves are frequently observed in patients with diabetes, with increasing prevalence in patients reporting symptoms of neuropathy.[8,9] Therefore, the so-called stocking-and-glove distribution of neuropathy might be explained by multiple compressed nerves in both the upper and lower extremities.[10] A potential cost-effective intervention is the surgical decompression of entrapped lower extremity nerves, of which health benefits and significant supportive clinical evidence have been previously reported.[11–13] More specifically, improvements in pain and sensation after lower extremity nerve decompression surgery resulted in fewer observed diabetic foot ulcerations and lower extremity amputations, compared to nonoperated subjects with diabetes.[12,14] These findings may eventually save lives, because ulceration is independently associated with death.[15] Despite these promising results, the long-term costs, health gains, and cost-effectiveness of lower extremity nerve decompression surgery have not been determined in a clinical study. A cost-effectiveness analysis is useful to evaluate the gain in health benefits for patients of a new treatment strategy compared to current care, to assess its "value for money," and to support health care policy decisions regarding insurance package coverage and reimbursement.[16] The aim of our study was to assess the long-term health benefits, cost consequences, and incremental cost-effectiveness of lower extremity nerve decompression surgery relative to current care in a group of diabetic patients with neuropathy at risk for lower extremity complications.

PATIENTS AND METHODS

Markov Model

A Markov model is a statistical technique to analyze uncertain processes over time. It is particularly useful when there is an ongoing risk over a longer time and when important events might occur more than once, as in diabetic foot complications. Therefore, Markov models are particularly suited to model the course of disease when events and the resulting consequences are likely to recur over time (e.g., long-term outcomes, costs, and effects).[17] A Markov model consists of two or more health states. The number and nature of the states are chosen regarding the health or decision problem[18]; that is, each health state is thought to be homogeneous in terms of resource use (costs) and health outcomes (effectiveness). Between two cycles, time progresses with one unit, and patients can transit between health states, stay in a health state, or die. The probability to stay in that state or move to another state is expressed as the transition probability. Through the cycles, the patients are followed individually over their lifetime.

Figure 1 shows our Markov model. It shows eight possible health states a diabetic subject may be confronted with during life, including neuropathy, diabetic foot ulcerations (uncomplicated, infected, or ischemic), primarily healed after ulceration, minor amputation, major amputation, and death (not separately displayed). All patients start their course of disease in the state "diabetes with neuropathy." We assumed that all lower extremity amputations are preceded by diabetic foot ulcerations, because diabetes underlies up to eight of 10 nontraumatic amputations, of which 85 percent are preceded by a diabetic foot ulceration.[19] Neuropathy symptoms are partially explained by the existence of multiple compression neuropathies.[20] We assume for this study that diabetic sensorimotor polyneuropathy and compression neuropathies do not render patients differently at risk regarding ulceration and consequent amputation.[21] Table 1 displays the 6-month transition probabilities used. The time horizon was 10 years or 20 cycles of 6 months. The 6-month cycle length corresponds to wound healing times, being between 2 and 8 months.[22]

Modeling Lower Extremity Nerve Decompression Surgery and Current Care

The model simulated two hypothetical cohorts of diabetic patients. The first cohort was modeled as patients with diabetes and neuropathy receiving lower extremity nerve decompression surgery, and the second was modeled as diabetic patients with neuropathy receiving current (nondecompression) care. For both cohorts, it was assumed that they received care for their feet according to international guidelines,[23] including prescription of analgesic drugs, mechanical offloading when necessary, treatment of peripheral artery disorders, and amputations when necessary. For the current care cohort, data were obtained from the Rotterdam Diabetic Foot Study, a prospective cohort study of unselected diabetic patients followed at the outpatient Diabetes Clinic

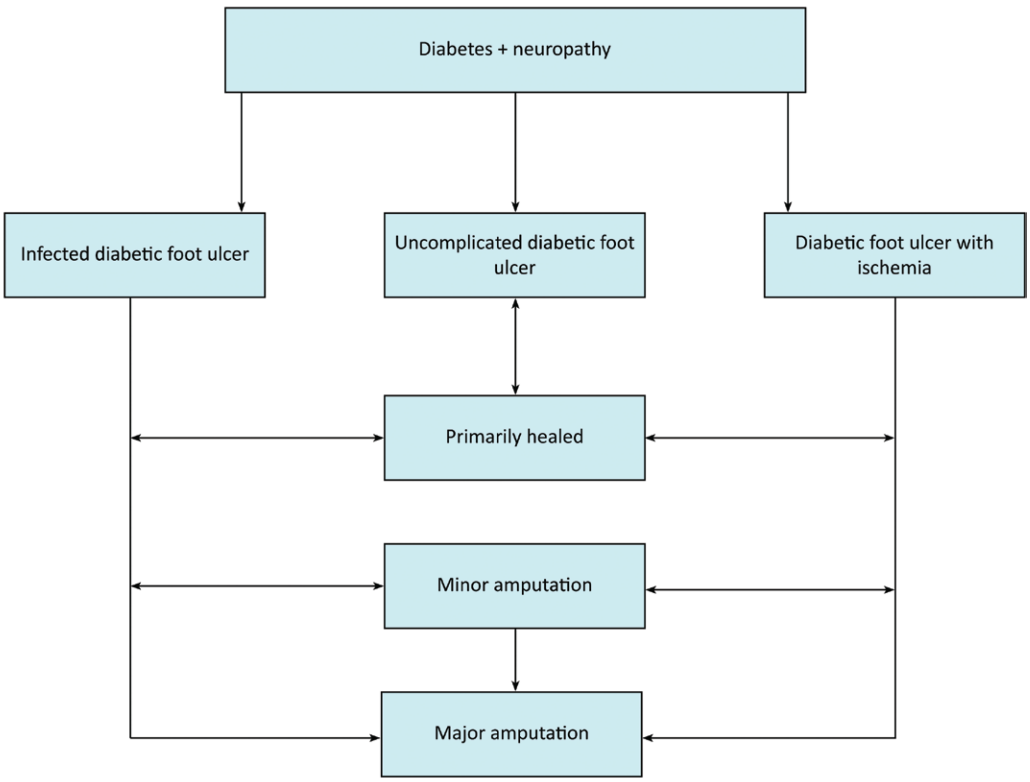

Fig. 1. Transition probabilities between health states in current care and after lower extremity nerve decompression surgery (cycle length, one-half year). Health states a diabetic subject with neuropathy may reside in ("death" is not displayed).

of Franciscus Gasthuis & Vlietland Hospital, Rotterdam, The Netherlands. The aim of the Rotterdam Diabetic Foot Study is to investigate the natural history of (compression) neuropathy, including deterioration of sensation of the feet. The Rotterdam Diabetic Foot Study design and methods have been described in detail.[9,24–26]

The model was illustrated using a base case of a 62-year-old diabetic patient with neuropathy caused by superimposed compression neuropathies of the lower extremities, diagnosed with the Tinel sign.[9] The mean age of diagnosis of diabetes corresponds to the mean age of Rotterdam Diabetic Foot Study patients; all patients of both cohorts were assumed to start in their 62nd year of life. To ensure consistency, data from comparable populations were preferred to feed the model.[17,27]

Data on effects and effectiveness of lower extremity nerve decompression surgery were retrieved from the literature.[12] Lower extremity nerve decompression surgery is carried out in patients with signs (i.e., a positive Tinel sign) of superimposed nerve compression of the tibial nerve at the tarsal tunnel, common fibular nerve near the head of the fibula, deep peroneal nerve at the dorsum of the foot, and superficial peroneal nerve just proximal of the ankle. The major indication for this intervention is relief of symptoms of neuropathy. The consequent gain in sensation at the feet, caused by tibial neurolysis, results in a lower likelihood of plantar diabetic foot ulceration and consequent lower extremity amputation.[28–31] Data from the literature were used to obtain incidence and prevalence rates of lower extremity complications for both cohorts (Table 1). Table 1 displays the consequent reduction in 6-month risks for lower extremity complications for the lower extremity nerve decompression surgery and current care cohorts.

Cost-Utility Analysis

After running, the Markov model reveals how many patients from the lower extremity nerve decompression surgery and current care cohorts have spent time in each health state. The main outcome measures were cumulative incidences of foot ulcers, minor and major amputations, and death after 10 years. Moreover, the cumulative (total) costs and quality-adjusted life-years after 10 years of treatment, and incremental cost-utility of lower extremity nerve decompression surgery versus current care, can be estimated once the costs

Table 1. Transition Probabilities between Health States in Current Care and after Lower Extremity Nerve Decompression Surgery*

		Transition Probability	
Health State		**Current Care**	**After LEND surgery**
Diabetes with neuropathy	Diabetes with neuropathy	0.95†	0.971165971‡
	Uncomplicated DFU	0.022†	0.000834028743894377§
	Infected DFU	0.014†	0.014†
	DFU with ischemia	0†	0
	Death	0.014‡	0.014‖
Uncomplicated DFU	Primary healed	0.9825†	0.9825†
	Death	0.0175†	0.0175‖
Infected DFU	Primary healed	0.4†	0.4‡
	Minor amputation¶	0.35†	0.35†‖
	Major amputation¶	0.09†	0.09†‖
	Death	0.16†	0.16‖
DFU with ischemia	Primary healed	0.38†	0.779332888‖
	Minor amputation¶	0.13†	0.000667111605597626§
	Major amputation¶	0.27†	0§
	Death	0.22†	0.22
Primary healed	Primary healed	0.803†	0.933354711‡
	Uncomplicated DFU	0.097†	0.018820637757194§
	Infected DFU	0.044†	0.00200401338690248§
	DFU with ischemia	0.029†	0.018820637757194§
	Death	0.027†‡	0.027‖
Minor amputation¶	Minor amputation	0.76#	0.76#
	Uncomplicated DFU	0.013#	0.013#
	Infected DFU	0.044†	0.044†
	DFU with ischaemia	0.029†	0.029†
	Major amputation	0.127‡	0.127‡
	Death	0.027†	0.027‖
Major amputation¶	Major amputation¶	0.88†	0.88‖
	Death	0.12†	0.12‖

LEND, lower extremity nerve decompression; DFU, diabetic foot ulcer.
*Cycle length, one-half year.
†Tennvall GR, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: A cost-utility analysis based on Markov model simulations. *Diabetologia* 2001;44:2077–2087.
‡Cumulative transition probability.
§Dellon AL, Muse VL, Nickerson DS, et al. Prevention of ulceration, amputation, and reduction of hospitalization: Outcomes of a prospective multicenter trial of tibial neurolysis in patients with diabetic neuropathy. *J Reconstr Microsurg.* 2012;28:241–246.
‖Same as current care transition probability.
¶An amputation could only be preceded by an infected or ischemic DFU.
#Ortegon MM, Redekop WK, Niesse LW. Cost-effectiveness of prevention and treatment of the diabetic foot: A Markov analysis. *Diabetes Care* 2004;27:901–907.

and utilities of each health state have been added. Cost-utility analysis was considered the appropriate framework because of the differences in health-related quality of life across the health states.

Costs

The cost-utility analysis took a hospital perspective (i.e., only included direct in-hospital costs). Considered were costs of in-hospital stay, consultancy costs, surgical interventions, microbiology and clinical laboratory tests, drugs, radiology, and pathology.[22] Costs were expressed in euros and whenever necessary adjusted to the 2015 price level using the consumer price index and discounted by 4 percent, in accordance with the Dutch guidelines for pharmacoeconomic research.[32] Annual costs were transformed to half-year values in agreement with the 6-month cycle in the Markov model. Table 2 displays an overview of the estimated resource use and costs per unit. The costs associated with the treatment of neuropathy was retrieved from the literature.[33] Costs of lower extremity nerve decompression

Table 2. Cost Estimates per Health State*

	6-Mo Average	
	Base Case	**Interquartile Range for Sensitivity Analyses**
Health state		
Diabetes with neuropathy	€574	€115–€746
Uncomplicated DFU	€10,145	€2102–€12,949
Infected DFU	€9545	€1722–€12,408
DFU with ischemia	€34,939	€12,958–€46,560
Primary healed	€10,145	€2102–€12,949
Minor amputation	€10,968	€2194–€14,259
Major amputation	€27,444	€5489–€35,677
Transition costs		
Minor amputation	€4107	€821–€5339
Major amputation	€7900	€1580–€10,270

DFU, diabetic foot ulceration.
*Costs are in euros (2015) and rounded. Costs for lower extremity nerve decompression surgery were €1400 plus €400 for surgical-site infections, which occur in 5.9% of operations.

surgery were derived from the financial department of the University Medical Center Utrecht (mean, €1435). Surgical-site infection associated with lower extremity nerve decompression surgery was accounted for, because this is reported to occur in 5.9 percent of diabetic patients.[12] Costs of surgical-site complications were derived from the literature (mean, €400).[34] A minority of patients suffer from worsening of neuropathy symptoms after surgery (5.6 percent). This can be caused by iatrogenic nerve injury or recurrent entrapment. Moreover, some patients do not experience positive effects of surgery but do not have worsening of symptoms (4 percent of patients).[12] In these circumstances, the continuation of analgesic drugs is required and was accounted for in the cohort simulation [0.056 × €236 (additional costs) per patient for six cycles].[33]

Utilities

Quality-adjusted life-year is the universal outcome measure in health care and the method of choice in cost-effectiveness studies. A quality-adjusted life-year is a combined measure of quality of life (life expectancy) and health-related quality of life. A quality-adjusted life-year is calculated as time spent in a health state times the utility or the valuation of that health state.[35] The utility score ranges from 0 (death) to 1 (perfect health); a higher utility score represents a better health state. Quality-adjusted life-years were transformed to 6-month values in agreement with the 6-month cycle length. Utility values were derived from the literature. Quality-adjusted life-years were discounted by 1.5 percent, following Dutch guidelines for pharmacoeconomic research (Table 3).[17,36,37]

Incremental Cost-Utility Ratio

The outcome of the cost-effectiveness study is the incremental cost-utility ratio, defined as the difference in (discounted) cumulative costs between lower extremity nerve decompression surgery and current care, divided by the difference in (discounted) cumulative quality-adjusted life-years between these strategies, and depicted in the cost-effectiveness plane. We also calculated the absolute cost-utility ratio of each strategy, the course of the incremental cost-utility ratio over time, the net monetary benefit (the linear combination of costs and effects, expressed in euros), and the net health benefit (expressed in quality-adjusted life-years).

To support decision-making, a willingness-to-pay threshold of €80,000 extra per quality-adjusted life-year gained was used, which represents the maximum amount the Dutch society is willing to spend to prolong life with 1 year of perfect health (i.e., €20,000 to €80,000 per quality-adjusted life-year gained, depending on the burden of disease).[38] We added a cost-effectiveness acceptability curve, which depicts the probability that a specific strategy is cost-effective at different thresholds of willingness-to-pay per quality-adjusted life-year.

Statistical Analyses

Absolute risk reduction and number needed to treat were calculated. Sensitivity analyses are an important part of cost-effectiveness analysis, because the method is based primarily on assumptions. Varying the model parameters is used to assess the robustness and validity of the incremental cost-utility ratio (point estimate) and other outcomes.[39] Probabilistic sensitivity analyses were performed on the effectiveness of lower extremity nerve decompression surgery, transition probabilities, transition costs, and utility weights, using 10,000 Monte Carlo simulations. Values were varied according to published data. The beta distribution was used for transition probabilities, the Gaussian distribution for utility weights, and the gamma distribution for costs. Microsoft Excel 15.14 (Microsoft Corp., Redmond, Wash.) and the R software (2019) with package markovchain (R Foundation for Statistical Computing, Vienna, Austria) were used for building the model.

Table 3. Health Utility Parameters per Health State

	Utilities (QALYs)	
Health State	Base Case	95% CI for Sensitivity Analyses
Diabetes with neuropathy	0.84	0.81–0.87
Uncomplicated DFU	0.75	0.71–0.79
Infected DFU	0.70	0.66–0.75
DFU with ischemia	0.59	0.53–0.65
Primary healed	0.60	0.51–0.69
Minor amputation	0.68	0.63–0.72
Major amputation	0.62	0.57–0.67

QALYs, quality-adjusted life-years; DFU, diabetic foot ulceration.

RESULTS

Base Case Analysis

Table 4 shows the impact of lower extremity nerve decompression surgery on the incidence of diabetic foot ulcers, minor amputations, major amputations, and death at 10-years follow-up (10,000 Monte Carlo simulations) for a 62-year-old diabetic patient with lower extremity compression neuropathies who is at risk for lower extremity complications. With lower extremity

Table 4. Ten-Year Cohort Stimulation Results Comparing the Incidence of Lower Extremity Complications between the Two Strategies

	Current Care (*n* = 10,000)		LEND Surgery (*n* = 10,000)		Risk Calculations*		
Health State	No. of Patients	Absolute Risk (%)	No. of Patients	Absolute Risk (%)	Absolute Risk Reduction (Risk Difference) (%)	Relative Risk	No. Needed to Treat
Diabetes with neuropathy†	3585	35.9	5570	55.7	−19.8	1.6	−5.0‡
Uncomplicated DFU	248	2.5	21	0.2	2.3	0.1	44.1
Infected DFU	137	1.4	88	0.9	0.5	0.7	206.2
DFU with ischemia	55	0.6	19	0.2	0.4	0.3	271.9
Primary healed	1663	16.6	780	7.8	8.8	0.5	11.3
Minor amputation	239	2.4	144	1.4	1.0	0.6	104.8
Major amputation	408	4.1	218	2.2	1.9	0.5	52.7
Death	3665	36.6	3160	31.6	5.0	0.9	19.8
Total DFUs§	440	4.4	128	1.3	3.1	0.3	32.0
Total amputations‖	647	6.5	362	3.6	2.9	0.6	35.1

LEND, lower extremity nerve decompression; ARR, absolute risk reduction; NNT, number needed to treat; DFU, diabetic foot ulcer.
*ARR or risk difference = risk (current care) − risk (LEND); RR = risk (LEND)/risk (current care); RRR = [risk (current care) − risk (LEND)]/risk (current care); NNT = 100/ARR.
†Not progressed to another health state.
‡Not clinically relevant.
§Aggregated number of patients from the health states uncomplicated DFU, infected DFU, and DFU with ischemia.
‖Aggregated number of patients from the health states minor amputation and major amputation.

nerve decompression surgery, approximately 55.7 percent of the simulated cohort remained in the health state "diabetes with neuropathy" (i.e., after surgery and thus with symptom relief), approximately 60 percent higher than current care (relative risk, 1.6). Moreover, with lower extremity nerve decompression surgery, a simulated 312 diabetic foot ulcerations (risk difference, 3.1; relative risk, 0.3) and 285 amputations (risk difference, 2.9; relative risk, 0.6) could be prevented compared to current care. The numbers needed to treat (with lower extremity nerve decompression surgery) to reverse risk for diabetic foot ulcers and amputations were 32.0 and 35.1, respectively.

Table 4 also shows that with lower extremity nerve decompression surgery, fewer patients will die within 10 years (risk difference, 5.0; relative risk, 0.9). The fewer observed lower extremity complications in the lower extremity nerve decompression surgery cohort resulted in less mortality and more lives saved compared to current care strategies (6335 versus 6840, respectively; or 505 lives saved in favor of lower extremity nerve decompression surgery) and, consequently, more (discounted) life-years saved (88,369.5 life-years versus 86,513.6 life-years; or 1855.9 life-years gained in favor of lower extremity nerve decompression surgery), and more discounted quality-adjusted life-years (67,652.5 quality-adjusted life-years versus 64,082.3 quality-adjusted life-years; or 3570.2 quality-adjusted life-years gained with lower extremity nerve decompression surgery), at lower discounted costs (€46,973 versus €68,172; or €21,199 saved with lower extremity nerve decompression surgery). Costs are initially higher for lower extremity nerve decompression surgery because of the costs of surgery and surgical-site infections in the first cycle but are surpassed by the costs of current care from 19 months onward.

Cost-Utility Analysis

Figure 2 shows the results of the probabilistic sensitivity analysis on the absolute and incremental cost-utility ratio when the parameter values are varied (Tables 1 through 3). Figure 3 shows the cost-effectiveness plane, visualizing the variation in incremental health effects and incremental costs for 10,000 iterations. Lower extremity nerve decompression surgery is likely to be less costly and more effective compared to current care (89.68 percent of iterations result in a position in the southeastern plane).

The incremental cost-utility ratio (point estimate) was −€59,279.6 per quality-adjusted life-year gained. The incremental cost-utility ratio is not only lower than the threshold of €80,000 per quality-adjusted life-year gained for societal decision-making, but it is also negative, implying that with lower extremity nerve decompression surgery instead of current care, costs on average are lower (€21,199) and quality-adjusted life-years on average are gained (3507.2). Lower extremity nerve decompression surgery is therefore the dominant strategy. Figure 4 shows the incremental cost-utility ratio over time, indicating that lower extremity nerve decompression surgery is the preferred option after 18 months.

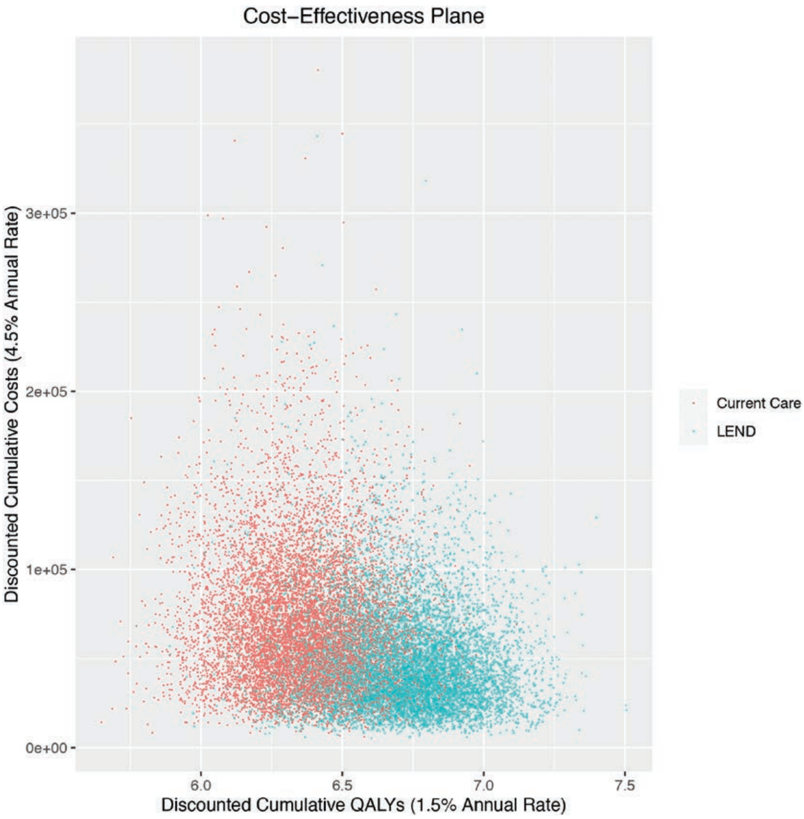

Fig. 2. Cost-effectiveness plane. Costs in euros (€). *QALY*, quality-adjusted life-year; *LEND*, lower extremity nerve decompression.

Figure 5, the acceptability curve, indicates that the probability for lower extremity nerve decompression surgery to be cost-effective is over 90 percent for any positive maximum amount that society is willing to pay for a quality-adjusted life-year. At a societal willingness-to-pay of €80,000, the net monetary benefit was €444,486.3 for current care and €494,246.9 for lower extremity nerve decompression surgery. The net health benefit was 6.4 versus 6.8. Both indicate that lower extremity nerve decompression surgery is the preferred strategy.

DISCUSSION

This study used a Markov decision model to project the epidemiologic outcomes and cost-effectiveness of two cohorts of diabetic subjects with nerve compression in the lower extremities, receiving either lower extremity nerve decompression surgery or current care. Our results suggest that lower extremity nerve decompression surgery is superior in relieving neuropathy symptoms and avoiding lower extremity complications, thereby saving life-years and improving quality of life, at lower costs. Both Dutch and U.S. health technology assessment criteria suggest that lower extremity nerve decompression surgery is a cost-effective strategy compared to the current care of diabetic subjects with neuropathy.[40]

Currently, the only viable treatments of neuropathy symptoms include analgesic drugs (e.g., anticonvulsants and tricyclic antidepressants), but these are not very effective and are associated with serious risks, and do not improve sensation in the insensate foot.[41] However, the high prevalence of treatable nerve entrapments in the lower extremity of diabetic subjects gave rise to a surgical approach to these refractory symptoms.[29,42] Despite being still controversial, cumulative data suggest an important role for the peripheral nerve surgeon in identifying the patient at risk, with consequent treatment recommendations.[20,43,44] The positive effects of lower extremity nerve decompression surgery are underscored by other studies from different research groups, on various outcome parameters,[45,46] including sensibility tests, balance, pain, nerve conduction studies, tibial nerve ultrasound, and electromyographic recordings. Moreover, these studies suggest that lower extremity nerve decompression surgery is safe with respect to risk of surgical-site infection (5.9 percent versus 9.5 percent in other types of

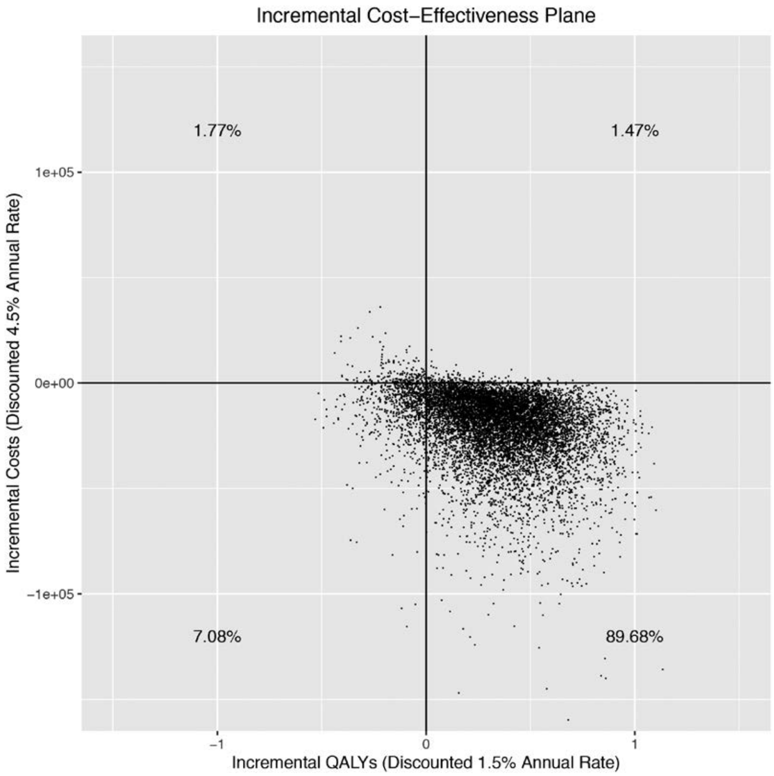

Fig. 3. Incremental cost-effectiveness plane. Costs in euros (€); *QALY*, quality-adjusted life-year.

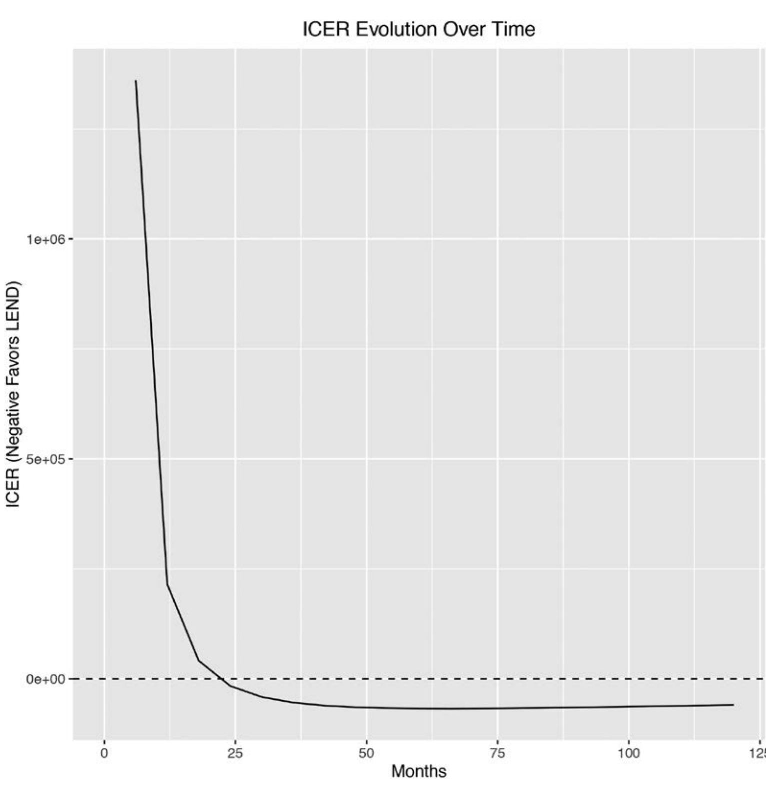

Fig. 4. Incremental cost-effectiveness ratio over time. *ICER*, incremental cost-effectiveness ratio; *LEND*, lower extremity nerve decompression.

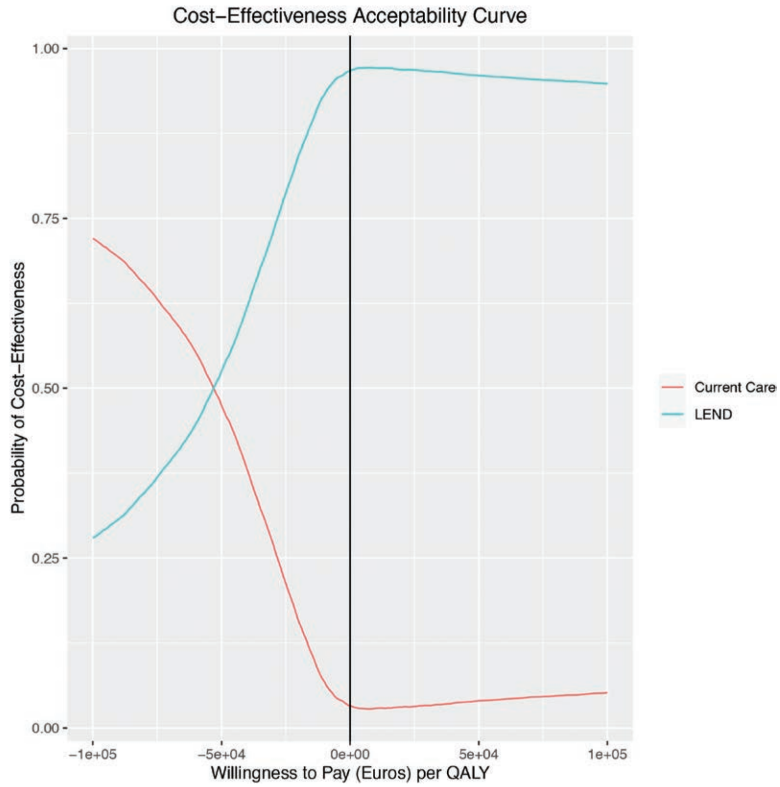

Fig. 5. Cost-effectiveness acceptability curve. *QALY*, quality-adjusted life-year; *LEND*, lower extremity nerve decompression.

lower extremity surgery), and infections that do occur are usually straightforwardly treated.[12,47] We included surgical-site infections in our model, and lower extremity nerve decompression surgery was cost-effective after month 18. Given this key result, we argue that a broader implementation of lower extremity nerve decompression surgery is possible. Multidisciplinary foot teams have proven to be cost-effective and are broadly available these days,[16,17,27,48] as are plastic surgeons and podiatrists with expertise in peripheral nerve surgery. Moreover, an epidemiologic study on the prevalence of tibial nerve compression showed that this condition is up to 61 percent more prevalent in diabetic subjects compared to nondiabetic controls.[9,21] Beyond the favorable cost-effectiveness of lower extremity nerve decompression surgery, out-of-hospital factors such as caregiver relief are probably significant.

Several caveats of our study are important to highlight. First, like any model, the validity of the results depends on the validity of the input data and the Markov model structure. The majority of the transition probabilities were derived from Swedish data, which roughly matched our population data, but was perhaps somewhat dated (years 2001 and 2004).[17,27,29] Moreover, only patients with neuropathy were modeled to undergo lower extremity nerve decompression surgery, because previous research suggested that only patients with mild to moderate nerve damage would benefit most from this type of surgery.[13] However, recent studies of decompression surgery in patients with a history of diabetic foot ulceration (although an indicator of end-stage nerve function) show that the recurrence risk of ipsilateral diabetic foot ulceration is lowered to 1.6 percent per year.[24,25,49] Treating this vulnerable group with lower extremity nerve decompression surgery could lead to an extra health gain. Only one study on lower extremity nerve decompression surgery in Tinel-negative subjects is known, and the surgical results are less successful compared to Tinel-positive subjects.[50] It is important to emphasize that the current literature on lower extremity nerve decompression surgery suggests that only Tinel-positive nerves should be operated on, in contrast to diabetic subjects with solely generalized peripheral neuropathy without nerve entrapments. Larger prospective studies should investigate these effects to corroborate (or redesign) the Markov model structure and its input data.[51]

Second, we did not include the costs and health effects of accidental falls in our analysis, which is an important source of disease burden and costs.[52] A previous report suggests an improvement of balance parameters to return to normal ranges after bilateral lower extremity nerve decompression surgery, which in turn could lower the risk of falls.[53] The improvement of lower extremity nerve decompression surgery on reinnervating the insensate foot likely has great potential to avoid falls. Unfortunately, we could not include this effect in our model because sensation was not measured in a uniform way, nor was this study prospective, and it did not report fall occurrence.

Finally, we included only the hospital-based costs, thereby disregarding medical costs outside hospitals, nonmedical patient-related costs, costs related to sick leave, and medical costs made during the life-years gained.[54] In part, we addressed this in the sensitivity analysis. We acknowledge that these costs can be considerable but they are also more difficult to estimate.[55] However, nonmedical costs, such as patient time and transportation costs are likely to be higher in the current care group, because the complications requiring hospital visits occur more frequently in this group. Medical costs during life-years gained are probably higher in the lower extremity nerve decompression surgery group. On balance, it is unclear whether the inclusion of these costs would have changed the overall cost difference.

CONCLUSIONS

Lower extremity nerve decompression surgery is highly effective and cost-effective in avoiding serious adverse events and is associated with a greater survival over time and less morbidity (better quality of life) in the long term. Large prospective studies can help to improve the model, especially the transition probabilities and utilities of the associated health states specific for lower extremity nerve entrapments. The overall conclusion that diabetic patients with neuropathy frequently have treatable nerve compression syndromes eligible for surgery provides guidance to the clinician. By examining the patient for nerve entrapments, a treatment option that affects long-term prognosis becomes available.

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